REMARKS/ARGUMENTS

The rejection of claims 75, 76, 78, 79, and 83 – 87 under 35 U.S.C. § 103(a) as being unpatentable over Anderson et al. (U.S. Patent No. 5,955,077) is respectfully traversed. As an initial matter, a favorable examination report in relation to the corresponding European patent application was very recently received. That examination report is in relation to a broader claim 1 as previously pending in the US in which SEQ. ID no. 1 is the only stated essential sequence and acknowledges novelty and inventive step over WO 95/01441 (the International Application corresponding to the US Patent of Andersen cited in this instance). Applicant would be glad to supplement the present remarks with copies of the EPO examination report although applicants well understand that US examiners are free to take a divergent approach from the EPO.

Turning now to the present rejection, a point taken by the Examiner handling the corresponding European Application but apparently not appreciated in the instant prosecution, is that Andersen does not direct selection of SEQ. ID No (the peptide designated ES1 corresponding to the N-terminal 15 amino acid fragment of ESAT-6) or any specific panel containing that peptide for diagnostic use in humans, while the data in the specification establishes the surprising finding that peptide ES1 alone detected about 60% of the human TB patients tested (lines 24-25 on page 1 of the description). This is comparable with a conventional skin test without the problem of false negatives arising from previous BCG vaccination. Addition of further peptides to accord with the claimed panel necessarily gives further improvement in both specificity and sensitivity, but the Andersen Patent provides no teaching to arrive at that precise panel which includes as a key component SEQ. ID No.1 and is more favored for use than whole EAST-6 since it will detect both $CD4^+$ and $CD8^+$ T cell responses. As stated in the last response and discussed in Example 6, whole ESAT-6 only detects $CD4^+$ T cell responses.

Moreover, the definition of "subsequence" at the top of column 6 of the Andersen Patent is particularly important in construing the teaching of the Andersen patent. That definition only clearly embraces polypeptides exhibiting identical or substantially identical properties to whole ESAT-6. As read with further definition of the term " subsequence" at lines 7 to 57 in the same column, the implication is that the a polypeptide "subsequence" is:

(a) a polypeptide with the same immunological characteristics as ESAT-6;

(b) a protein with similar amino acid composition; and

(c) a functionally and /or immunolgically ***equivalent*** protein.

A T cell–presenting epitope peptide such as ES1 is not immunologically equivalent to ESAT-6. The reference at lines 49-52 in column 5 to polypeptides of "at least 12 amino acids long, preferably at least 15 amino acids long" is no direction to select any specific short peptide. It merely provides speculative guidance on a minimal starting point for identifying subsequences which are identical or substantially identical in immunological properties to ESAT-6.

Furthermore, vague references to subsequences comprising a T cell epitope in the Andersen Patent cannot be seen as direction to provide a panel of peptides as required by pending claim 75. This is particularly so when it is noted that section (b) of claim 1 of the Andersen patent proposes to test for subsequences relying on T cells from mice- infected with tuberculosis. Such a test using animal T cells is not suitable for identifying any human epitopes. Please note that D7 provides data showing that a peptide from the C-terminal region of ESAT-6, peptide p8, is effective in a skin test in detecting T cells in guinea pigs infected with *M. tuberculosis,* while peptide p1 (amino acid residues 1-20 of ESAT-6) gave no significant result in the same test scenario.

The only example in the Andersen Patent concerning diagnosis is Example 6 which reports skin testing of purified whole ESAT-6 in guinea pigs. The specification provides no teaching whatsoever that assists in selecting a panel of peptides with high specificity and sensitivity for human diagnostic use in humans as specified in claim 75.

The Examiner has suggested the need for some improvement feature to be explicitly written into the claims. However, this perhaps relates to the fact that the Examiner sees the Andersen Patent as far closer to the claims than warranted. In brief, Andersen had no concept of a diagnostic test having clinical utility based on short T cell-epitope-containing ESAT-6 fragments. As stated in an earlier response, filed September 24, 2004, the Andersen Patent does little more than confirm that whole ESAT-6 will produce a T cell response when utilized in a skin test in guinea pigs. This is a long way from identification of a specific panel of peptides for *in vitro* human diagnosis which detected 96% of TB patients tested (line 3, page 20 of the description)

While applicants' comments in previous responses remain apt, it is believed that the present comments further demonstrate that the claims should be allowable. If the Examiner still disagrees, a telephone call to applicants' attorney is respectfully requested to enable applicants to fully understand the Examiner's position.

Respectfully submitted,

Robert Berliner
Registration No. 20,121

Tel.: (213) 892-9237
Fax: (213) 892-9494